IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Wang et al.	)	
		)	
Filed:	November 21, 2003	)	
		)	Group Art Unit: 1641
Serial No.:	10/719,868	)	
		)	Examiner: Ceperley, Mary
Title:	Method and Composition Useful in the Determination of FK506	)	
		)	Date: November 10, 2006
Attorney Docket:	DCS-9082	)	

INTERVIEW SUMMARY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In a telephonic interview with the Examiner during the week of October 27, 2006, the Examiner noted that the printers requested correction to the specification as follows:

1 The word "Figure" for Figures 1-4 should be deleted or otherwise corrected. To comply, the amendment to the specification enclosed herewith replaces "Figure" with "Formula" at paragraphs [0002], [0012], [0013], [0014] and [0034].

2. Figure 5 should be submitted as a drawing in compliance with 37 CFR § 1.84. To comply Figure 5 is renumbered as Figure 1 and submitted herewith as a drawing in compliance with 37 CFR §1.84.

Please note that the Printer's requirements are not currently on the PAIR system. This submission adds no new matter and is being submitted electronically

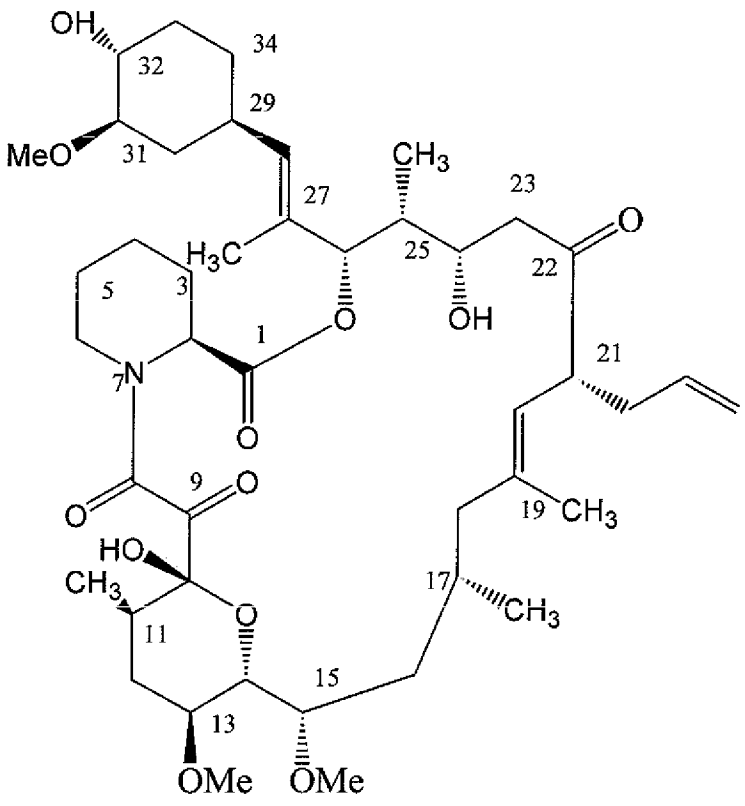
AMENDMENT

In the Specification:

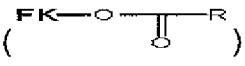
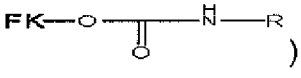
Replace paragraph [0002] with the following replacement paragraph which is marked to show all changes relative to the previous version.

[0002] FK 506 (or tacrolimus) is a cyclic, poly-N-methylated undecapeptide, possessing immunosuppressive activity. FK 506 is a macrolide immunosuppressant that is produced by Streptomyces tsukubaensis No 9993 The structure of FK 506 is shown in ~~Figure~~ Formula 1.

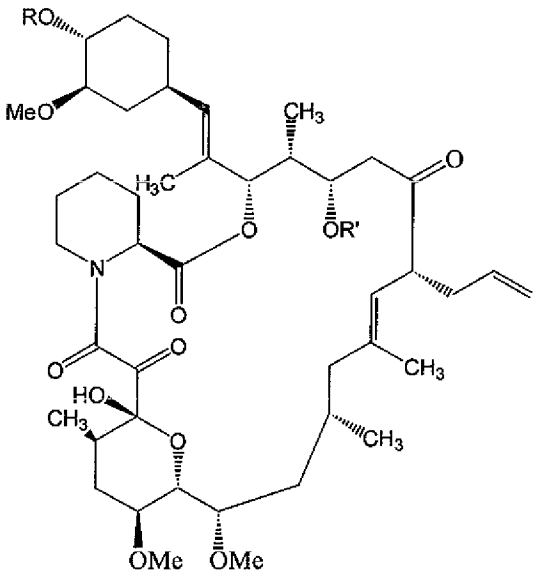
~~Figure~~ Formula 1



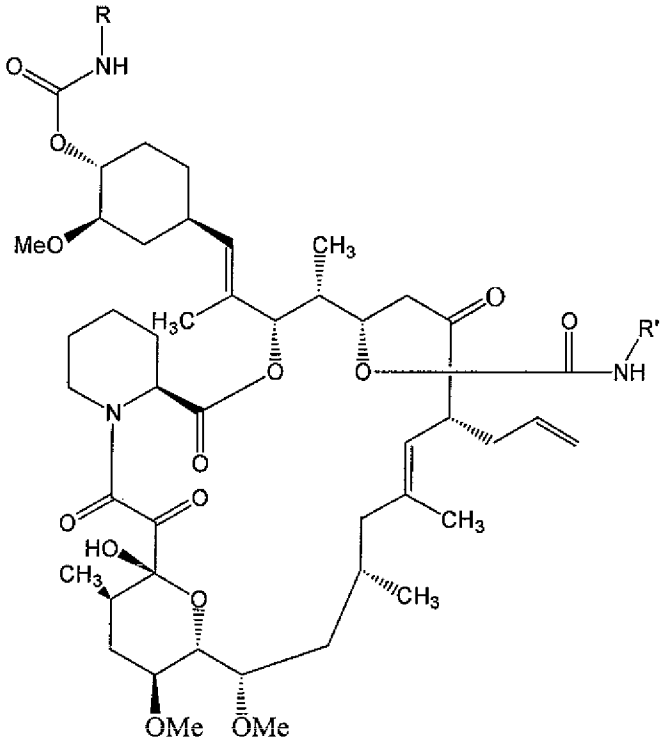
Replace paragraph [0012] with the following replacement paragraph which is marked to show all changes relative to the previous version.

[0012] The FK 506 derivatives of the present invention are prepared by derivatizing tacrolimus The derivatives are formed at the -OH groups of tacrolimus, at C-32 and/or C-24 to form ether, (FK-OR), ester (), or carbamate linkages () providing derivatives of FK-506 at either or both of these positions. In one aspect both the C-32 and C-24 are derivatized and in another aspect the derivatives are di-carbamate derivatives. Thus, the substances of the present invention may be for example the derivatives exemplified in ~~Figure~~ Formula 2. R (at C-32) and R' (at C-24) may be independently selected from alkyl or allyl groups from C1 to C25, either linear or branched or aromatic groups with or without substitutions In addition the alkyl, allyl or aromatic group may contain other functional groups such as ester, ethers, amides, acyl, amines, hydroxyl, sulfonates, phosphates, sulfates, phosphonate groups and the like. R may not be H. R' may be H. Many of these derivatives are known in the art. See, for instance, U.S. 5,665,727.

~~Figure~~ Formula 2



~~Figure~~ Formula 3

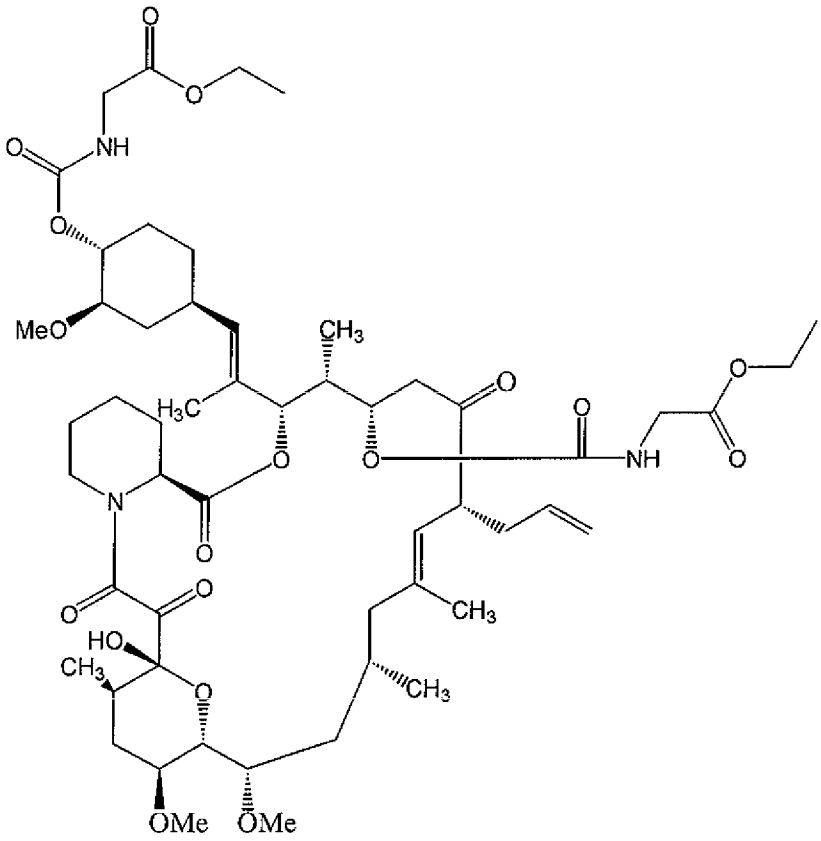


Replace paragraph [0013] with the following replacement paragraph which is marked to show all changes relative to the previous version.

[0013] Other aspects of the invention are shown in ~~Figure~~ Formula 3 above . These carbamate derivatives are derivatized at both C-24 and C-32. R and R' may be independently selected from alkyl, allyl, acyl, aryl in addition the alkyl, allyl, or aromatic group may contain other functional groups such as ester, ethers, amides, acyl, sulfonates, phosphates, sulfates, phosphonate groups and the like.

R may be H. R' may be H

~~Figure~~ Formula 4



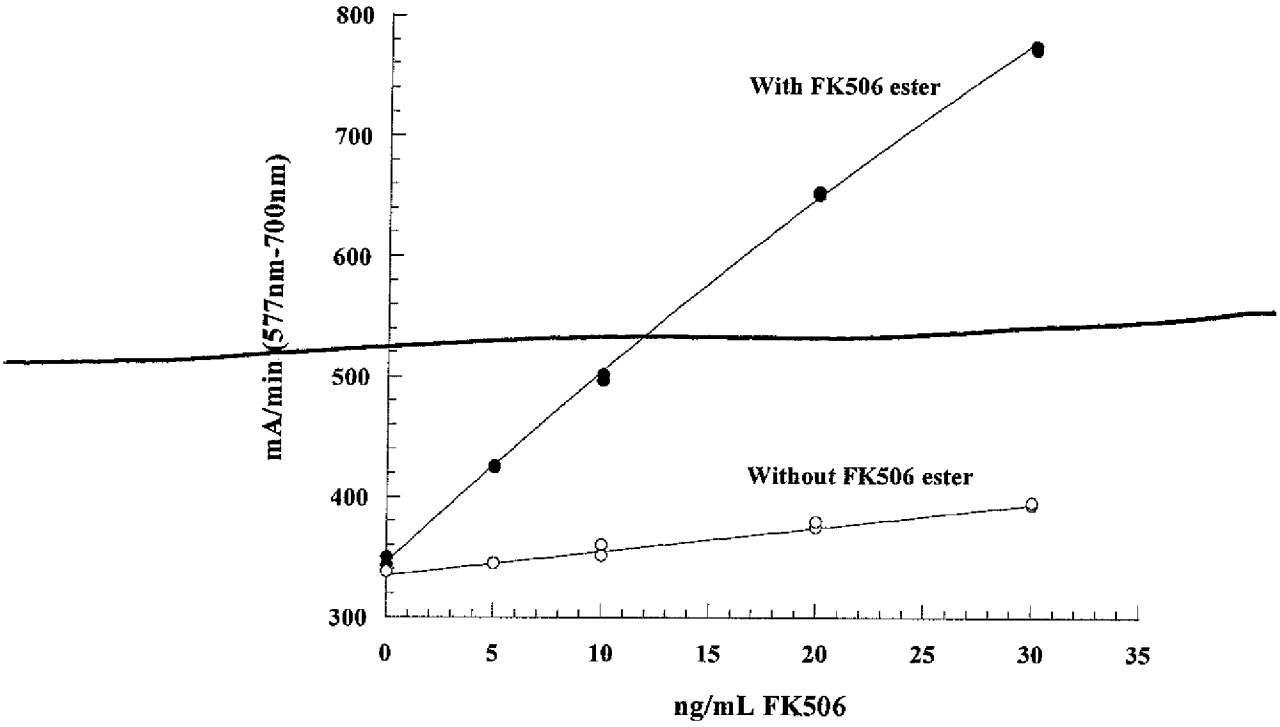
Replace paragraph [0014] with the following replacement paragraph which is marked to show all changes relative to the previous version.

[0014] A particular carbamate derivative is shown above in ~~Figure~~ Formula 4. This carbamate derivative is derivatized at both C-24 and C-32. In this example R and R' are identical

Replace paragraph [0034] with the following replacement paragraph which is marked to show all changes relative to the previous version. The Figure is deleted from the text and is being submitted as a drawing.

[0034] The measurement of FK506 used the assay format known as ACMIA and as described in the previous patents (US 5147529, US 5128103, US 5158871, US 4661408, US 5151348, US 5302532, US 5422284, US 5447870, US 5434051). The principle and operation of the FK506 method are as follows: pretreatment reagent containing the FK506 carbamate described in this invention is added to the reaction vessel on the Dimension® chemistry RxL/HM instrument. Next 35 µLs of whole blood containing FK506 is added The whole blood is sampled from a standard cup by first mixing the blood with the ultrasonic sample probe. The mixing of whole blood sample with the FK506 carbamate pretreatment solution ensures the lysis of the whole blood and the displacement of the protein bound FK506 molecules from their binding sites by the FK506 carbamate molecules. The released FK506 molecules therefore will be accessible to the anti-FK506 antibody in the reaction mixture. Anti-FK506 antibody-β-galactosidase conjugate (80 uL) is added next and allowed to react with FK506 in the sample. The chrome particles with immobilized FK506-BGG (bovine gamma globulin)-dextran is added (75uL) and allowed to bind the unreacted conjugate. The FK506 bound Anti-FK506 antibody-β-galactosidase conjugate does not bind to the chrome but remains in the supernatant when a magnetic field is applied to the above reaction mixture to separate the solution from the chrome particles. The FK506 bound conjugate is detected by transferring the supernatant from the reaction vessel to a photometric cuvette, and measuring the enzymatic rate of the conjugate in the presence of chlorophenol red-β-D-galactopyranoside (CPRG). The rate is measured bichromatically at 577 and 700 nm. The method schematic is provided in the figure ~~below~~.

Typical calibration curves with and without the FD506 carbamate pretreatment are compared as shown in ~~Figure 5~~ Figure 1.



~~Figure 5. Representative calibration curves representing the DIMENSION® assay treated with or without the FK506 carbamate pretreatment.~~

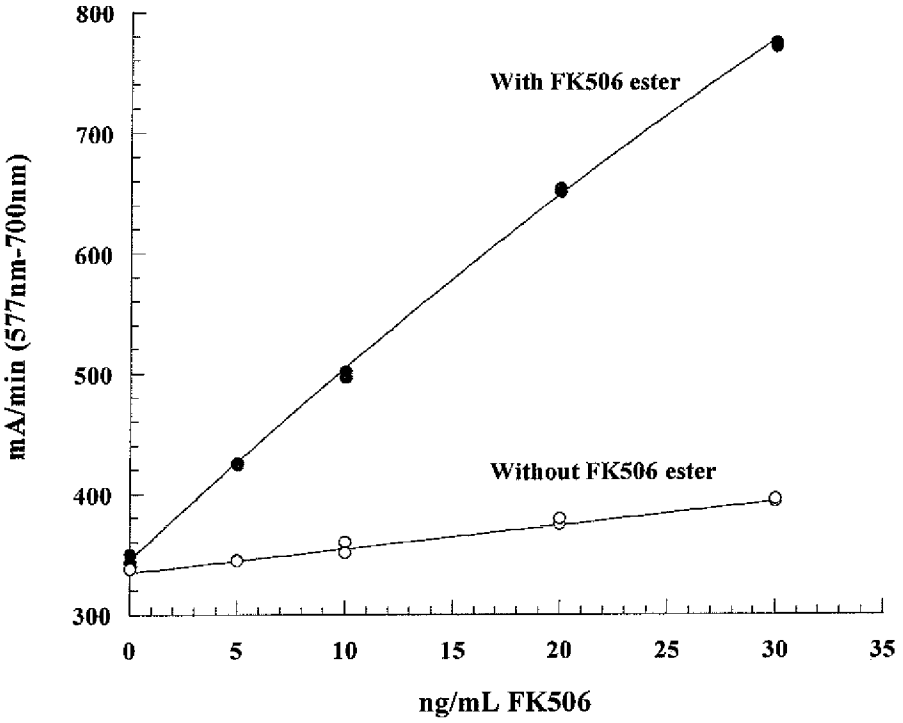
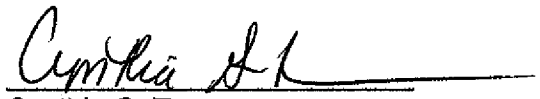


Figure 1. Representative calibration curves representing the DIMENSION® assay treated with or without the FK506 carbamate pretreatment.

Applicants submit that the amendments comply with the printer's requirements. The Examiner is encouraged to contact the undersigned if the Examiner has any matter that she would like to address.

Respectfully submitted,



Cynthia G. Tymeson
Registration No. 34,745
Attorney for Applicants

Dade Behring Inc.
Legal Dept. - Patents
1717 Deerfield Rd.
Deerfield, IL 60015
Phone: 302-631-0360